Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade - DTU Orbit (08/11/2017)

Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade

As tumors grow, they acquire mutations, some of which create neoantigens that influence the response of patients to immune checkpoint inhibitors. We explored the impact of neoantigen intratumor heterogeneity (ITH) on antitumor immunity. Through integrated analysis of ITH and neoantigen burden, we demonstrate a relationship between clonal neoantigen burden and overall survival in primary lung adenocarcinomas. CD8(+)tumor-infiltrating lymphocytes reactive to clonal neoantigens were identified in early-stage non-small cell lung cancer and expressed high levels of PD-1. Sensitivity to PD-1 and CTLA-4 blockade in patients with advanced NSCLC and melanoma was enhanced in tumors enriched for clonal neoantigens. T cells recognizing clonal neoantigens were detectable in patients with durable clinical benefit. Cytotoxic chemotherapy-induced subclonal neoantigens, contributing to an increased mutational load, were enriched in certain poor responders. These data suggest that neoantigen heterogeneity may influence immune surveillance and support therapeutic developments targeting clonal neoantigens.

General information

State: Published
Organisations: National Veterinary Institute, Section for Immunology and Vaccinology
Authors: McGranahan, N. (Ekstern), Furness, A. J. S. (Ekstern), Rosenthal, R. (Ekstern), Andersen, S. R. (Intern), Lyngaa, R. B. (Intern), Saini, S. K. (Intern), Jamal-Hanjani, M. (Ekstern), Wilson, G. A. (Ekstern), Birkbak, N. J. (Ekstern), Hiley, C. T. (Ekstern), Watkins, T. B. K. (Ekstern), Shafi, S. (Ekstern), Murugaesu, N. (Ekstern), Mitter, R. (Ekstern), Akarca, A. U. (Ekstern), Linares, J. (Ekstern), Marafioti, T. (Ekstern), Henry, J. Y. (Ekstern), Van Allen, E. M. (Ekstern), Miao, D. (Ekstern), Schilling, B. (Ekstern), Schadendorf, D. (Ekstern), Garraway, L. A. (Ekstern), Makarov, V. (Ekstern), Rizvi, N. A. (Ekstern), Snyder, A. (Ekstern), Hellmann, M. D. (Ekstern), Merghoub, T. (Ekstern), Wolchok, J. D. (Ekstern), Shukla, S. A. (Ekstern), Wu, C. J. (Ekstern), Peggs, K. S. (Ekstern), Chan, T. A. (Ekstern), Hadrup, S. R. (Intern), Quezada, S. A. (Ekstern), Swanton, C. (Ekstern)
Pages: 1463-1469
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information

Journal: Science
Volume: 351
Issue number: 6280
ISSN (Print): 0036-8075
Ratings:

BFI (2017): BFI-level 2

Web of Science (2017): Indexed yes

BFI (2016): BFI-level 2

Scopus rating (2016): CiteScore 14.39 SJR 13.535 SNIP 7.688

Web of Science (2016): Indexed yes

BFI (2015): BFI-level 2

Scopus rating (2015): SJR 12.906 SNIP 7.826 CiteScore 13.12

Web of Science (2015): Indexed yes

BFI (2014): BFI-level 2

Scopus rating (2014): SJR 12.012 SNIP 8.269 CiteScore 12.68

Web of Science (2014): Indexed yes

BFI (2013): BFI-level 2

Scopus rating (2013): SJR 12.305 SNIP 7.87 CiteScore 12.43

ISI indexed (2013): ISI indexed yes

Web of Science (2013): Indexed yes

BFI (2012): BFI-level 2

Scopus rating (2012): SJR 13.159 SNIP 8.124 CiteScore 12.39

ISI indexed (2012): ISI indexed yes

Web of Science (2012): Indexed yes

BFI (2011): BFI-level 2

Scopus rating (2011): SJR 14.049 SNIP 8.309 CiteScore 11.97

ISI indexed (2011): ISI indexed yes

Web of Science (2011): Indexed yes

BFI (2010): BFI-level 2

Scopus rating (2010): SJR 13.216 SNIP 7.791
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 11.644 SNIP 7.033
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 10.996 SNIP 6.09
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 9.871 SNIP 6.021
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 10.337 SNIP 6.052
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 10.834 SNIP 6.581
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 11.249 SNIP 7.255
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 11.106 SNIP 7.371
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 10.5 SNIP 7.071
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 10.853 SNIP 6.907
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 12.983 SNIP 7.088
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 16.117 SNIP 7.073
Original language: English
DOIs:
10.1126/science.aaf1490
Source: FindIt
Source-ID: 2298450552
Publication: Research - peer-review › Journal article – Annual report year: 2016